PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
P37336WO/TF		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/002845	01.07.2004	01.07.2003

International Patent Classification (IPC) or national classification and IPC
A61K7/40, A61K7/42

Applicant
HYGIEIA PHARMACEUTICALS LIMITED et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 8 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.01.2005	08.11.2005

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/002845

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1, 2, 4-6, 8-10, 12-33	as originally filed
3, 3a, 7, 11	received on 27.05.2005 with letter of 27.05.2005
Claims, Numbers	
1-20	received on 27.05.2005 with letter of 27.05.2005
Drawings, Sheets	
1/3-3/3	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 21,22
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 16-18

because:

☒ the said international application, or the said claims Nos. 16-18 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/002845

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	19,20
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20
Industrial applicability (IA)	Yes:	Claims	1-15,19,20
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- The subject-matter of claims 16-18 is related to a method for treatment of the human or animal body from surgery or therapy. Using its discretion, the present authority decided not to carry out an international preliminary examination on that subject-matter (Article 34(4)(a)(I) PCT in conjunction with Rule 67.1(iv) PCT).

For the assessment of the present claims 16-18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 - The following documents (D1,D2,D3) are referred to in this communication (Article 33(6) PCT); the numbering will be adhered to in the rest of the procedure:

D1: US-A-5 648 083 (DECKNER GEORGE ENDELL ET AL) 15 July 1997 (1997-07-15)

D2: US-B-6 387 3821 (SALEH MICHAEL ET AL) 14 May 2002 (2002-05-14)

D3: US-A-5 208 013 (KLEIN KENNETH) 4 May 1993 (1993-05-04)

2. Novelty (Article 33(2) PCT)

a - The subject-matter of present claims 1-18 is considered as novel over the cited prior art (Article 33(2) PCT):

None of the cited documents D1-D3 refers to a barrier formulation as described in present claim 1 which comprises an emulsion having an oil phase comprising a silicone compound and an aqueous phase, the viscosity of the formulation being 20 Pascal second (20000 cps) or less and the formulation further comprising an active ingredient selected from triclosan and

alexidine present in an amount from 0.5-10% by weight of the formulation.

b - The subject-matter of present claims 19,20 is considered as not novel over the cited prior art for the following reasons (Article 33(2) PCT):

- Document D1 describes a personal care formulation and a method of manufacturing said formulation, which comprises an emulsion having an oil phase comprising a silicone compound and an aqueous phase, the formulation further comprising an active ingredient, and one or more emollient, excipient, a thickener, an emulsifier, a preservative agent and a neutralising agent or pH-adjusting agent (Cf. D1, column 3, line 30-line 51; column 4, line 11-column 5, line 28; column 7, line 23-column 8, line 14; column 8, line 36-line 66; column 11, line 18-line 33).
The subject-matter described in document D1 takes away novelty of present claims 19,20.

- Document D2 refers to a composition for skin care protection an a method of manufacturing said formulation which comprises an oil phase comprising a silicone compound and an aqueous phase, the formulation further comprising an active ingredient, and one or more emollient, excipient, a thickener, an emulsifier and a neutralising agent (Cf. D2, column 1, line 60-line 65; column 2, line 39-column 3, line 2; column 4, line 3-line 19; claims 1-5).
The subject-matter described in document D2 takes away novelty of present claims 19,20.

3. Inventive Step (Article 33(1),(3) PCT)

a - Since the subject-matter of present claims 19,20 is known, it can obviously not be considered as inventive (Article 33(1),(3) PCT).

b - The remaining subject-matter, which is the subject-matter of present claims 1-18 cannot be considered as inventive for the following reasons (Article 33(1),(3) PCT):

- The subjective problem to be solved by the present application is to provide a barrier formulation which keeps its properties during a long time after application and which does not have to be frequently re-applied.

- The solution proposed in the present application is a barrier formulation as described in present claim 1.

- Document D3, which is considered as the closest prior art, describes a composition for skin care and protection which comprises an oil phase comprising a silicone compound and an aqueous phase, the formulation further comprising an active ingredient, and one or more emollient, excipient, a thickener, an emulsifier and a preservative agent (Cf. D3, column 1, line 60-line 65; column 2, line 39-column 3, line 2; column 4, line 3-line 19; claims 1-5).

- The difference between the teaching of the closest prior art and present claim 1 is the presence of an active agent selected from triclosan and alexidine present in an amount from 0.5-10% by weight of the formulation.

- The technical effect of this difference is the provision of a barrier formulation with an antibacterial agent.

- This feature is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.
Therefore, the subject-matter of present claims 1-18 does not involve an inventive step according to Article 33(1),(3) PCT.

- Claims 16-18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

4. Industrial Application (Article 33(4) PCT)

- The subject-matter of present claims 1-15,19,20 is considered to be industrially applicable; claims 1-15,19,20 therefore, satisfy the criterion set forth in Article 33(4) PCT.

CLAIMS

1. A barrier formulation which comprises an emulsion having at least an oil phase comprising a silicone compound and an aqueous phase, the viscosity of the formulation being 20 Pascal second (20000 cps) or less, and the formulation further comprising an active ingredient selected from triclosan and alexidine present in an amount from 0.5 to 10% by weight of the formulation, and one or more of an emollient, an excipient, a thickener, an emulsifier, a neutralising agent, a preservative, and water.

2. A formulation as defined in claim 1 wherein the silicone compound is a silicone fluid.

3. A formulation as defined in claim 2, wherein the silicone fluid is selected from dimethicone, a silicone emulsion, a dimethicone cross polymer, and a polydimethylsiloxane.

4. A formulation as defined in any one of the preceding claims, which comprises from 0.1 to 10% by weight, from 0.5 to 5% by weight, or from 1% to 2% by weight of the silicone compound.

5. A formulation as defined in any one of the preceding claims, wherein the active ingredient is present in an amount from 1 to 5% by weight, or about 2% by weight of the formulation.

6. A formulation as defined in any one of the preceding claims which further comprises a fragrance.

7. A formulation as defined in any one of the preceding claims, wherein the formulation comprises the following ingredients in the ranges indicated:

Ingredient	Range (wt%)
Castor oil	0.5-3.0
Stearic acid	0.5-8.0
Glycerol stearate	0.1-3.0
Cetyl palmitate	0.1-2.0
Silicone fluid	0.1-10
Nipastat	0.1-0.5
Jojoba oil	0.1-0.5
Liquid paraffin	0.1-0.5
Active ingredient	0.5-10
Water	35-95
Carbomer	0.5-8.0
Aloe vera	0.1-2.0
Monopropylene glycol	2.0-15
Triethanolamine	0.1-2.0

8. A barrier formulation as defined in any one of the preceding claims, for use as a skin barrier for humans or animals.

9. A barrier formulation as defined in any one of claims 1 to 7, for use in medicine, including veterinary medicine.

10. Use of a formulation as defined in any one of claims 1 to 7, in the manufacture of a medicament for use in the treatment and/or prophylaxis of infections.

11. Use of a formulation as defined in claim 10, wherein the medicament is for use in the treatment and/or prophylaxis of skin infections.

12. Use of a formulation as defined in claim 10, wherein the medicament is for use in the treatment and/or prophylaxis of hospital acquired infections.

13. Use of a formulation as defined in claims 10 or 11, wherein the medicament is for use in the treatment and/or prophylaxis of skin infections in animals.

14. Use of a formulation as defined in claim 13, wherein the medicament is for use in the treatment and/or prophylaxis of mastitis infection and/or the spread of mastitis infection between farm animals.

15. Use of a formulation as defined in claim 13, wherein the medicament is for use in the treatment and/or prophylaxis of teat sores in animals

16. A method for the treatment and/or prophylaxis of skin conditions, the method comprising applying a barrier formulation as defined in any one of claims 1 to 7 to the skin.

17. A method for the treatment and/or prophylaxis of infection, the method comprising applying a barrier formulation of any one of claims 1 to 7 to a human or animal.

18. A method for the treatment and/or prevention of hospital acquired infections, the method comprising administering a barrier formulation as defined in any of claims 1 to 7 to a health care worker.

19. A method of manufacturing a formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound which method comprises the steps of:

(a) preparing an oil phase containing a silicone compound;

(b) preparing an aqueous phase;

(c) mixing the oil phase and the aqueous phase together;

(d) neutralising the mixture with a neutralising agent.

20. A method as defined in claim 19 wherein the water phase is added to the oil phase to obtain an oil-in-water emulsion.

compliance with hand hygiene and despite many initiatives, new ways of ameliorating this problem have been sought.

According to a first aspect of the invention, there is provided a barrier formulation which comprises an emulsion having at least an oil phase comprising a silicone compound and an aqueous phase, the viscosity of the formulation being 20 Pascal second (20000) cps or less, and the formulation further comprising an active ingredient, and one or more of an emollient, an excipient, a thickener, an emulsifier, a neutralising agent, a preservative, and water.

The present invention also provides a barrier formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound wherein the viscosity of the formulation is 20 Pascal second (20000 cps) or less.

According to a second aspect of the invention, there is also provided a method of manufacturing a formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound which method comprises the steps of:

(a) preparing an oil phase containing a silicone compound;

(b) preparing an aqueous phase;

(c) mixing the oil phase and the aqueous phase together;

(d) neutralising the mixture with a neutralising agent.

According to a further aspect of the invention, there is provided a barrier formulation of the invention for use as a skin barrier.

The formulation according to the invention has been found to act as an effective skin barrier to irritants and/or allergens. In particular, it has been found to be possible to apply concentrated sulphuric acid to the skin of a person which has been pre-treated with the formulation according to the invention with no ill effects to the person's skin.

Indeed the formulation of the invention has been found to prevent and/or reduce contact dermatitis and other skin conditions in workers such

The method may be for treating and/or preventing skin infections in animals. The method may comprise applying a barrier formulation of the invention to the skin of an animal. The method may be for treating and/or preventing mastitis infection of and/or the spread of mastitis infection between cattle. The method may alternatively be for the treatment and/or prophylaxis of teat sores in farm animals.

In a further aspect there is provided a method for the treatment and/or prophylaxis of damaged skin, the method comprising applying the barrier formulation of the invention to the damaged skin. Therefore the formulation may be applied to wounds to promote wound healing such as for treating scrapes, grazes, cuts, scalds and/or burns formed in the skin.

The silicone compound may be a silicone fluid. The silicone fluid may be dimethicone, a silicone emulsion, a dimethicone cross polymer, or a polydimethylsiloxane. The silicone fluid may be silicone fluid 200/100 CS. The formulation according to the invention may comprise from 0.1 to 10% by weight, from 0.5 to 5% by weight, or from 1% to 2% by weight of the silicone compound .

The formulation according to the invention may be in the form of a lotion in order to be easy to apply and to dispense, particularly in a hospital or veterinary environment. The viscosity of the formulation may be from 1 Pascal second (1000 cps) to 20 Pascal second (20000 cps). The viscosity of the formulation may be from 1 Pascal second (1000 cps) to 5 Pascal second (5000 cps).

The formulation according to the invention may comprise an active ingredient. The active ingredient may be included in the oil or water phase depending on in which phase it has greater solubility.

The active ingredient may be:

- a chemical or physical sun protection agent (e.g. ethylhexyl methoxycinnamate, 4-methylbenzylidene camphor, octyldimethyl PABA, avobenzone, benzophenone-3, octacrylene, titanium dioxide, zinc oxide, and any combination thereof);

acrylic acid crosslinked with an allyl ether of pentaerythritol, and allyl ether of sucrose, or an allyl ether of propylene.

A suitable neutralising agent for use in the method of the invention is an alkaline agent. The neutralising agent may be triethanolamine, sodium hydroxide or potassium hydroxide.

The formulation may comprise the following ingredients in the ranges indicated:

Ingredient	Range (wt%)
Castor oil	0.5-3.0
Stearic acid	0.5-8.0
Glycerol stearate	0.1-3.0
Cetyl palmitate	0.1-2.0
Silicone fluid	0.1-10
Nipastat	0.1-0.5
Jojoba oil	0.1-0.5
Liquid paraffin	0.1-0.5
Active ingredient	0.5-10
Water	35-95
Carbomer	0.5-8.0
Aloe vera	0.1-2.0
Monopropylene glycol	2.0-15
Triethanolamine	0.1-2.0

The formulation may be prepared in the following steps:

1. Melting together the castor oil, stearic acid, glycerol stearate, cetyl palmitate, silicon fluid, jojoba oil, liquid paraffin and Nipastat.
2. Ensure the above a mixed together well and heat to between 70-80 °C.
3. In a separate vessel mix together the monopropylene glycol, triethanolamine, 50% of water and carbomer.